Neuroimaging with MRI: Some of the Things We Can See

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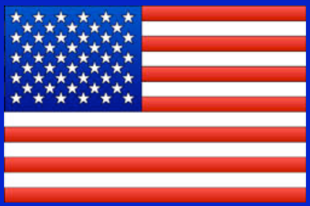
Scientific and Statistical Computing Core

DIRP / NIMH / NIH / DHHS / USA / Earth



06 Dec 2007

Preview of Coming Attractions

- Quick overview of MRI physics (all on one slide!)
- Some images and their applications
  - T1-weighted = gray/white/CSF delineation
  - T2-weighted = detection of tissue abnormalities
  - T2*-weighted = venography
  - Contrast agents
    - Enhancement of signals from various tissue types/conditions
    - DCEMRI & tumor quantification
  - Diffusion weighted imaging = white matter quantification
- Imaging brain function with MRI
- Brain atlases and statistical neuroanatomy

Synopsis of MRI

1) Put subject in big magnetic field [and leave him there]

⇒ Magnetizes the H nuclei in water ($\mathbf{H}_2O$)

2) Transmit radio waves into subject [about 3 ms]

⇒ Perturbs the magnetization of the water

3) Turn off radio wave transmitter

4) Receive radio waves re-transmitted by subject's H nuclei

⇒ Manipulate re-transmission by playing with H magnetization with extra time-varying magnetic fields during this readout interval [10-100 ms]

⇒ Radio waves transmitted by H nuclei are sensitive to magnetic fields — those imposed from outside and those generated inside the body:

⇒ Magnetic fields generated by tissue components change the data and so will change the computed image

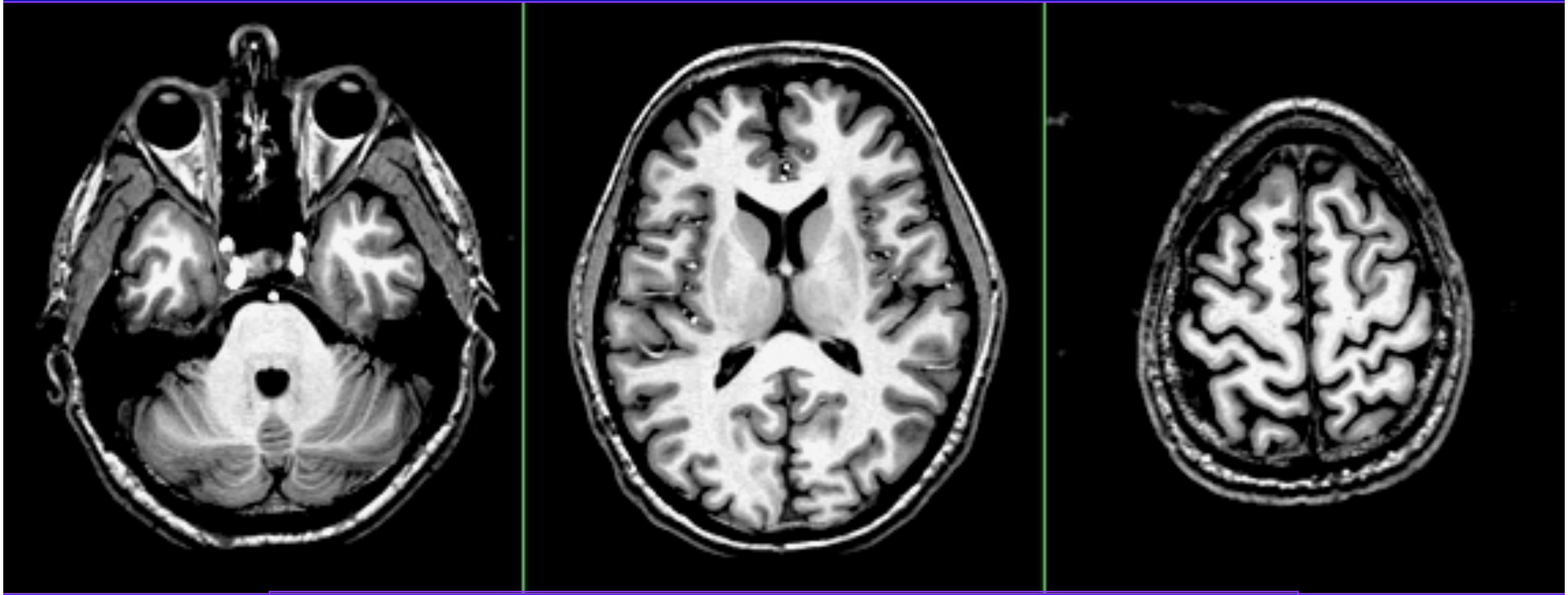
5) Store measured radio wave data vs time

⇒ Now go back to **2**) to get some more data [many times]

6) Process raw ("*k*-space") radio wave data to reconstruct images

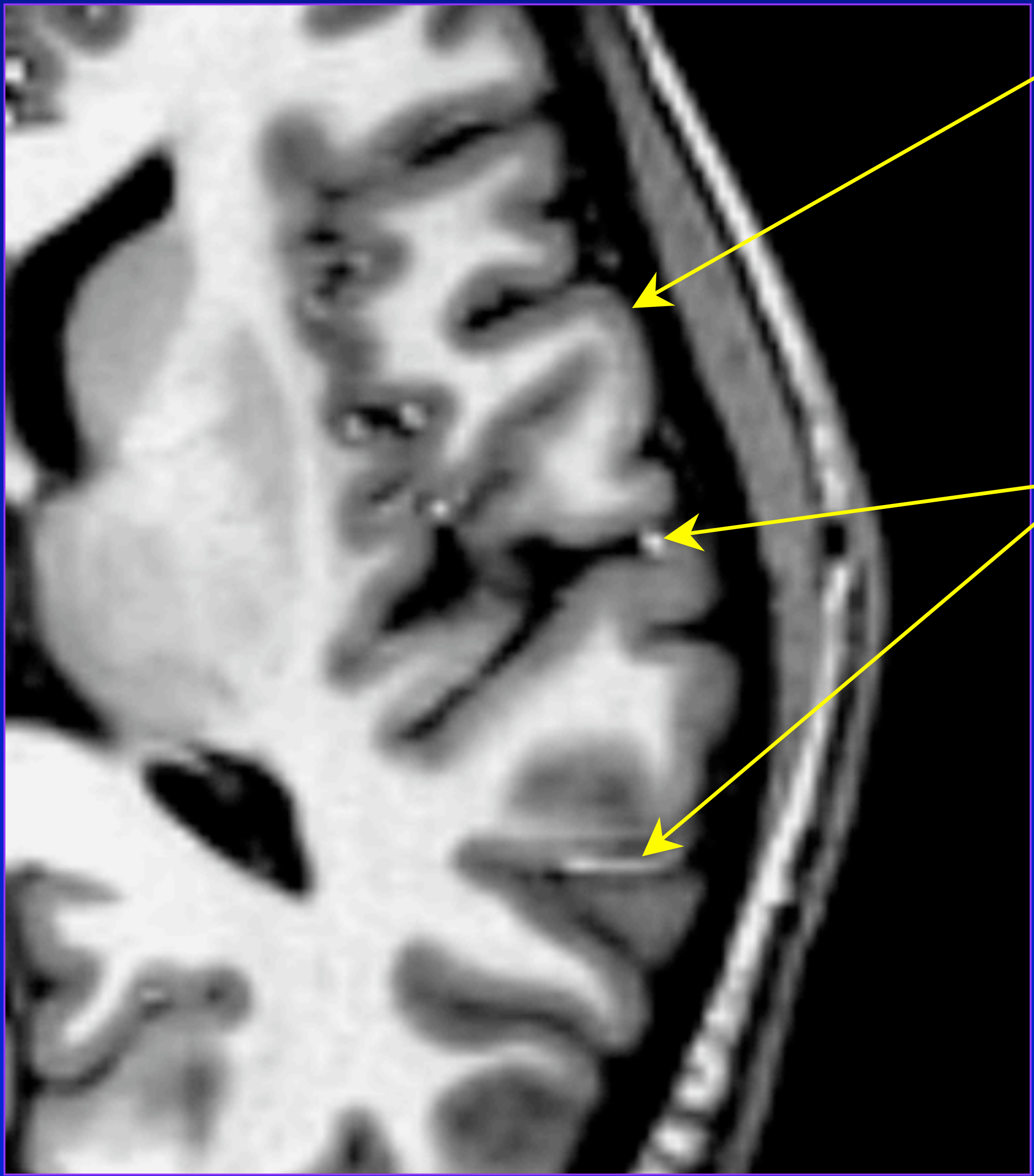
T1-Weighted Images

- Images whose design (timing of radio pulses and data readout) is to produce ***contrast*** between gray matter, white matter, and CSF



Three axial (AKA transaxial or horizontal) slices:
Spatial resolution is about 1 mm^3
Acquisition time for whole head is 5-10 minutes

Zooming In

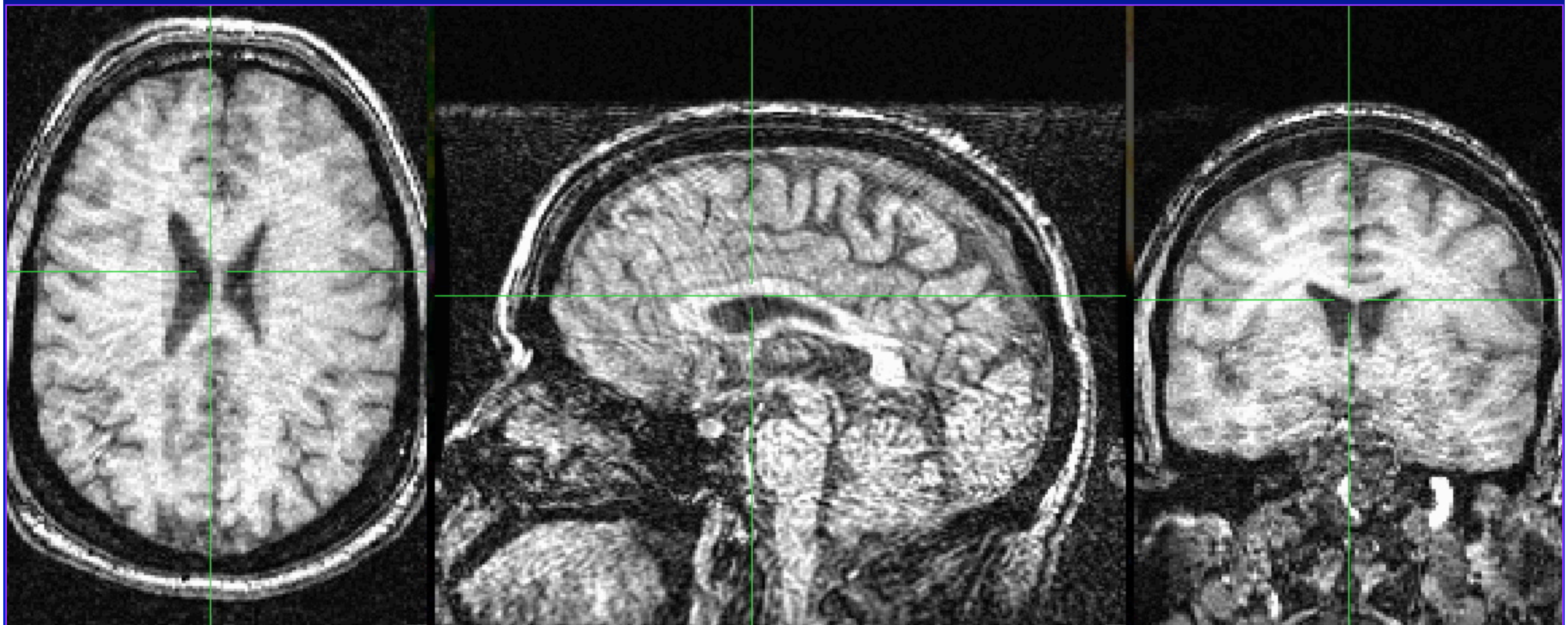


- Can follow GM cortex fairly well
  - Can measure thickness of cortex and try to quantify vs age and/or disease and/or genes
- Bright spots and lines: arterial inflow artifact
  - Leads to idea of MRA = Magnetic Resonance Angiography = acquire images to make arteries stand out even more
- Higher spatial resolution is possible
  - At the cost of scan time

Three Slices from a Volume

- A single acquisition is somewhat noisy
- Previous T1-weighted image was actually average of 4 separate acquisitions (to average out noise)
- MRI can be a 2D or a 3D acquisition technique

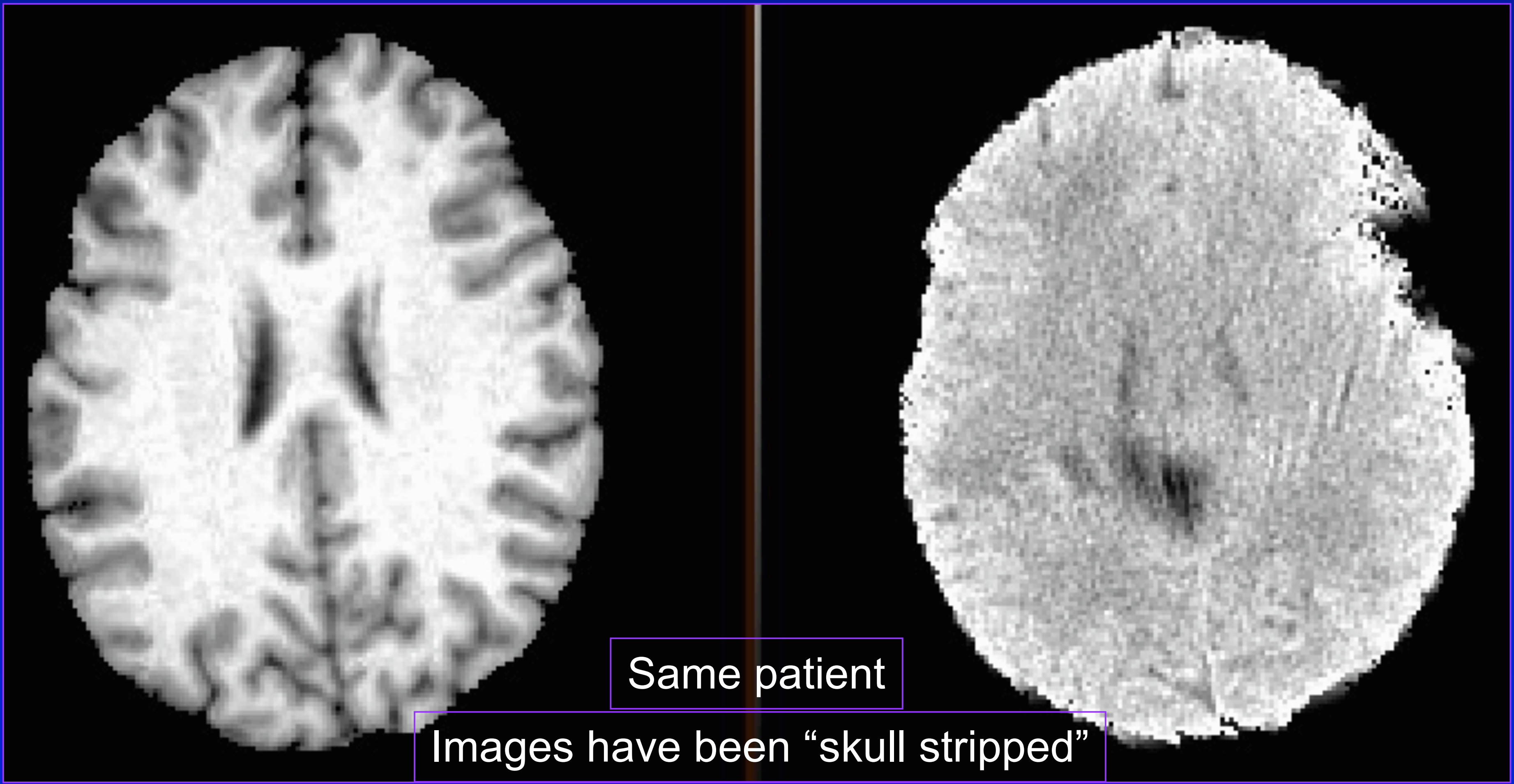
Some Bad MR Images



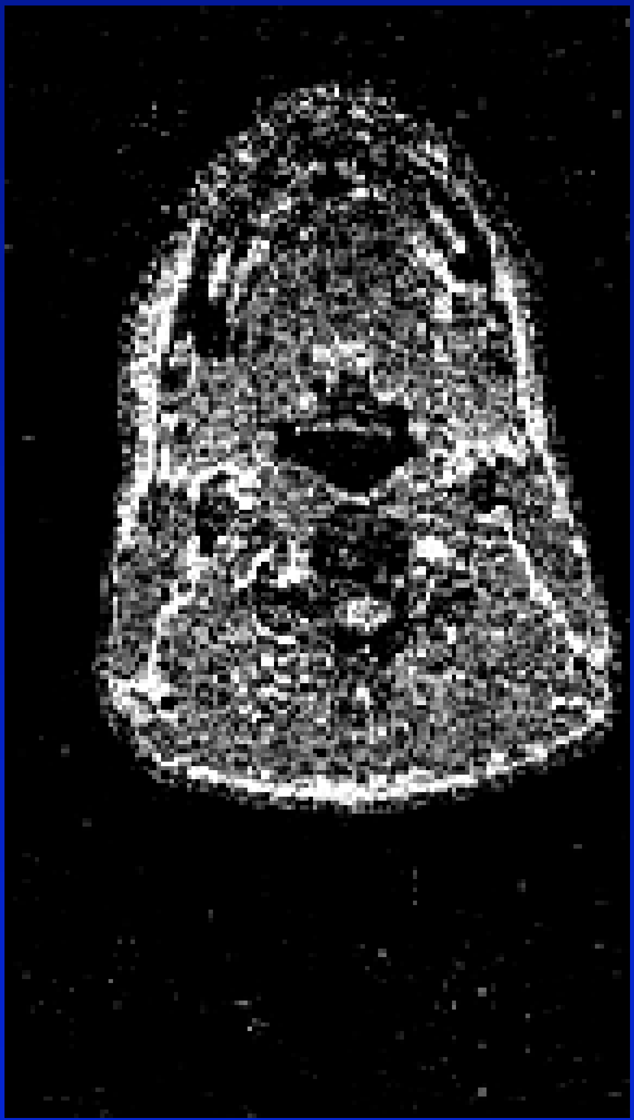
- Subject moved head during acquisition
  - Ghosting and ringing artifacts
  - Might be OK for some clinical purposes, but not much use for most quantitative brain research

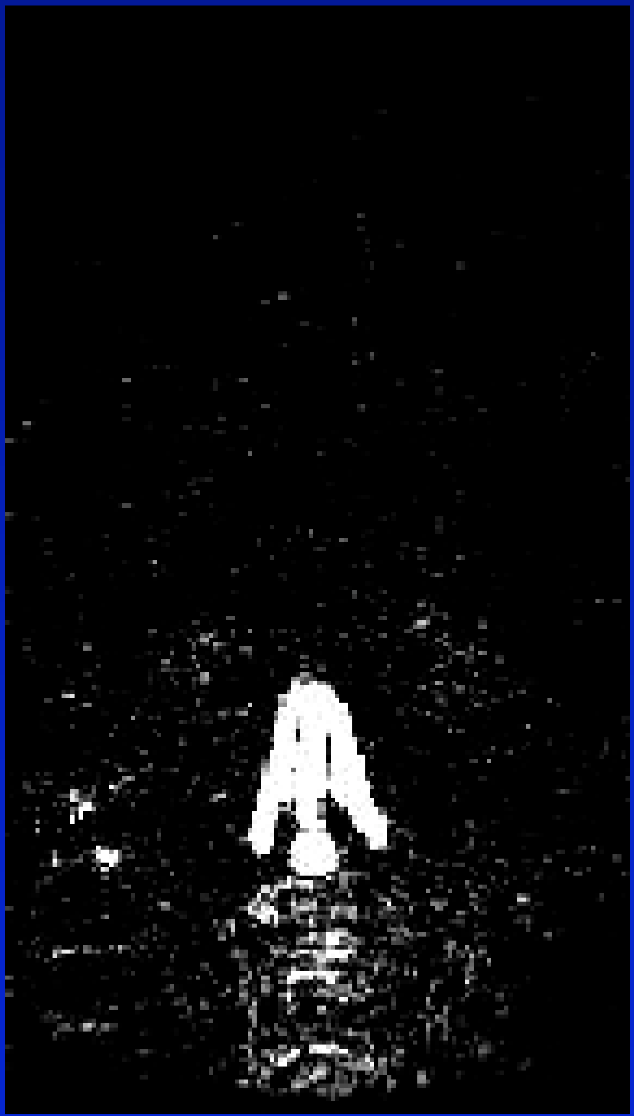
MRI vs CT in the Brain

- Skull gets in the way of X-ray imaging:
  - Bone scatters X-rays much more than soft tissue
  - MRI radio waves pass unimpeded through bone



Brain Slice Animations



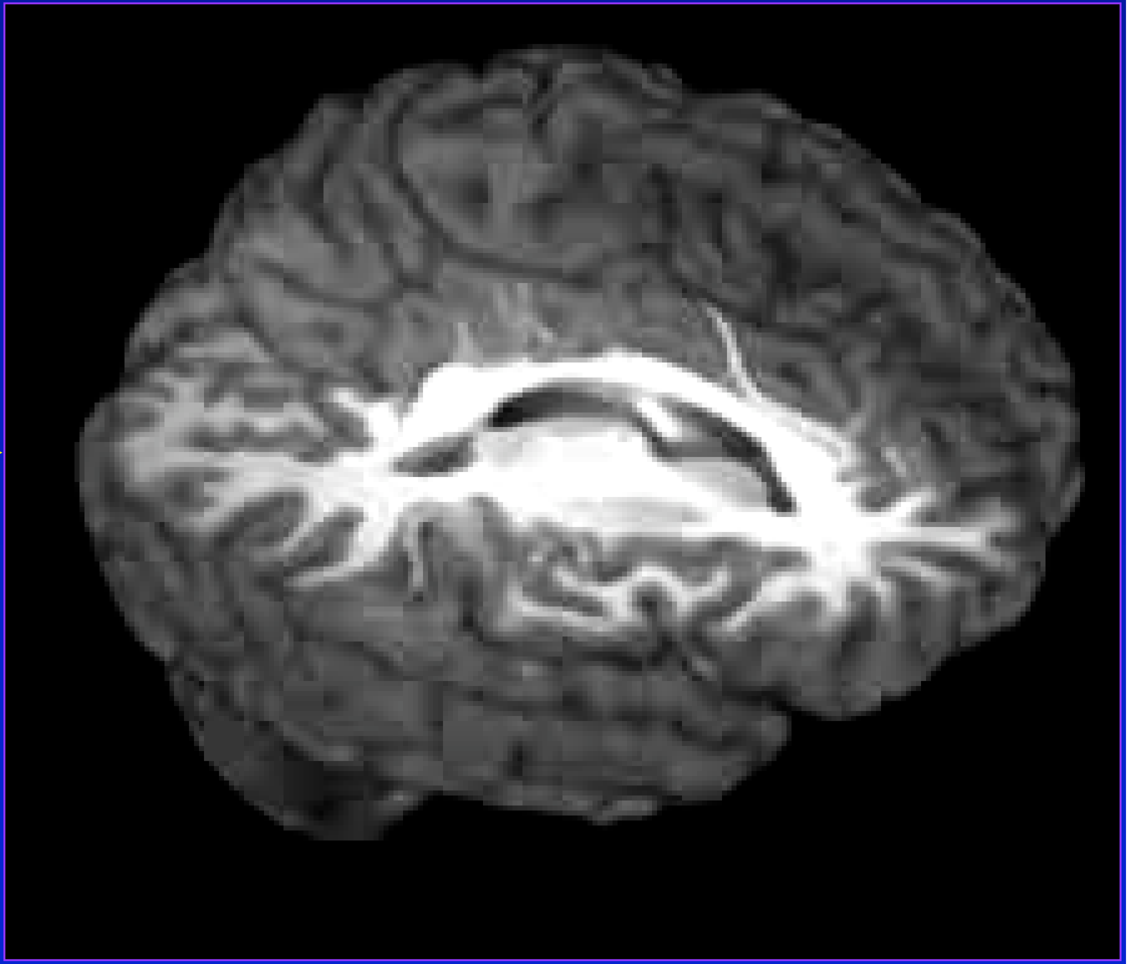


- Fun to watch (brain soup)
- More useful if movement through slices is under your direct interactive control

3D Visualization

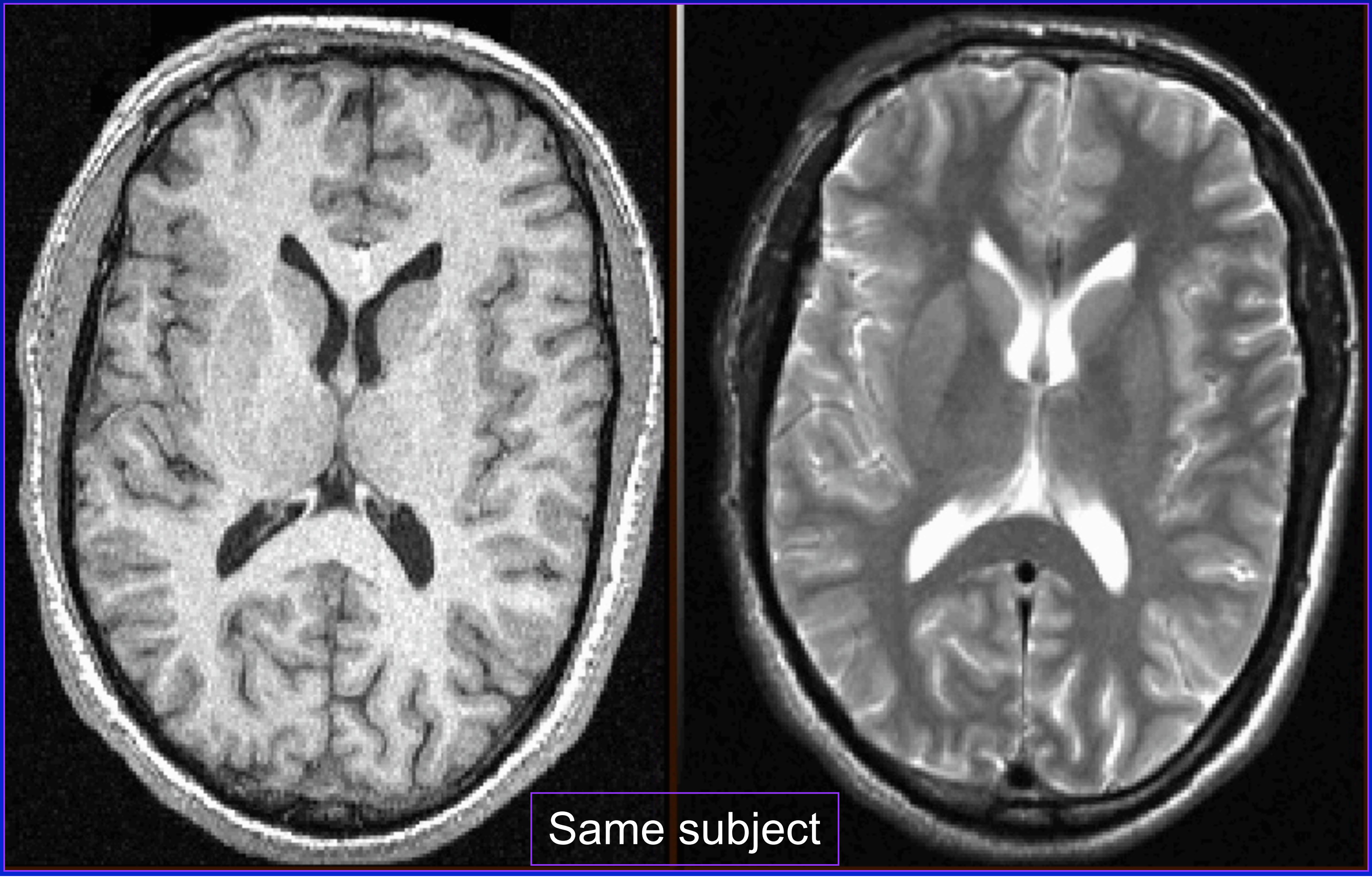
- MR images are 3D, but screens and retinas are 2D
- Understanding 3D structures requires looking at them in different ways

Volume rendering of T1-weighted image showing how corpus callosum spreads into hemisphere



T2-Weighted Images

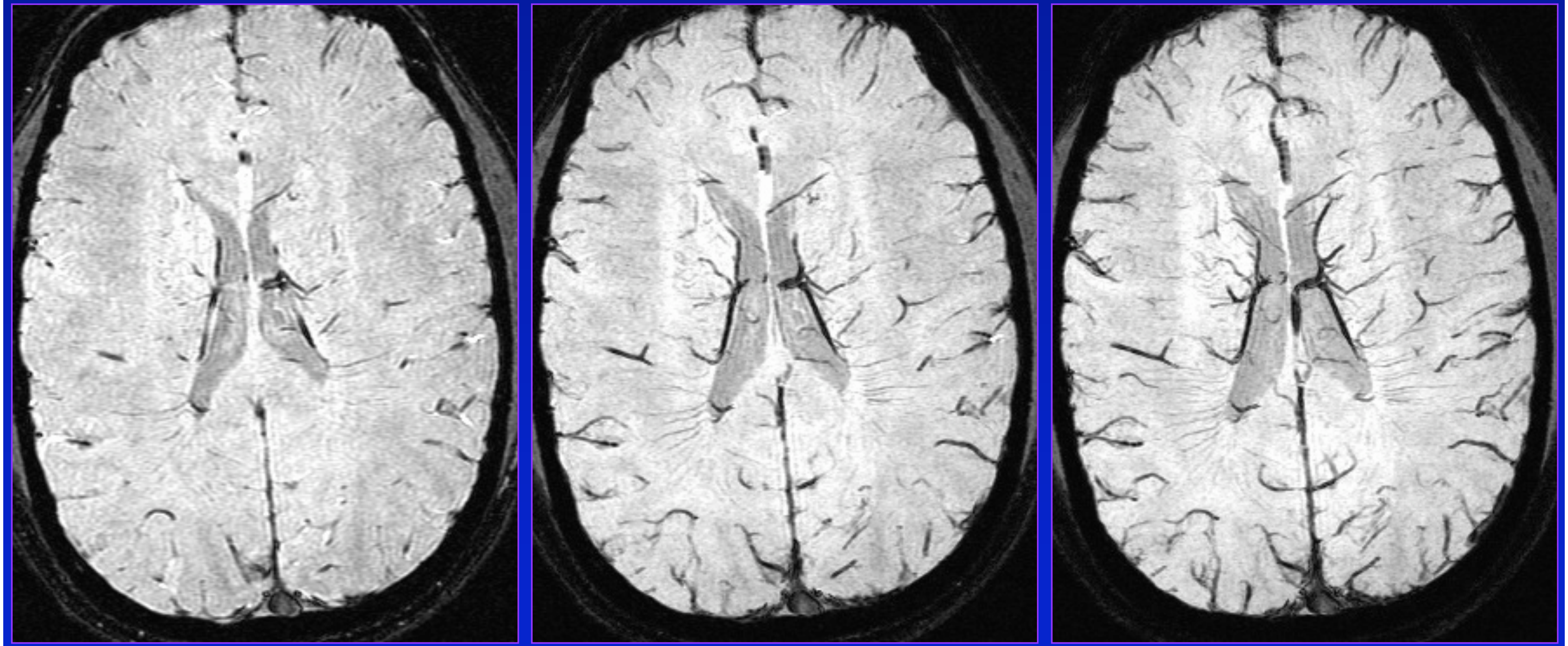
- Often better than T1-weighting in detecting tumors and infarcts (usually radiologists look at both types of scans)



Same subject

T2*-Weighted Images

- Designed to make venous blood (with lots of deoxy-hemoglobin) darker than normal tissue = *venography*



Output image

minIP ±1 slice

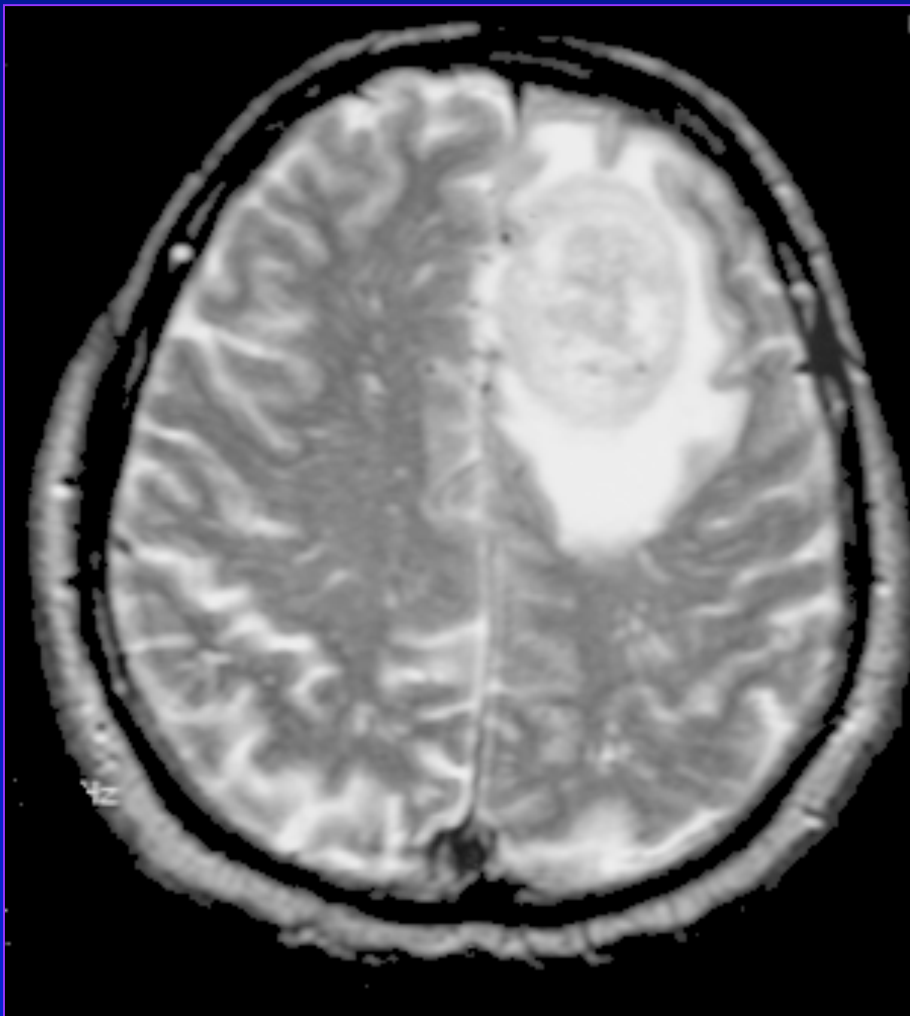
minIP ±2 slices

Images post-processed to enhance small effects

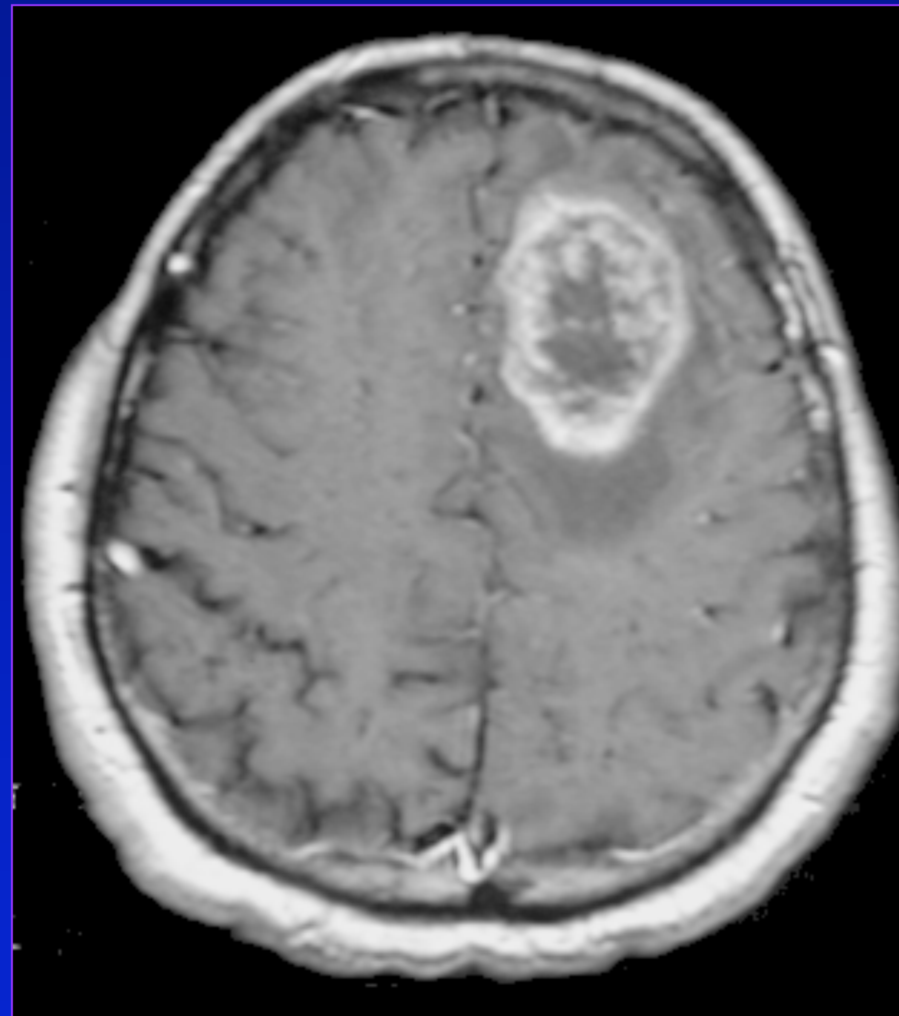
MRI Contrast Agents

- Chemicals injected into blood, designed to alter MRI signal by affecting magnetic environment of H nuclei
  - Developed starting in late 1980s (and still continuing)
  - Used millions of times per year in USA
  - Designed to be biologically inert (only “active” magnetically)
    - About 1 person in 100,000 has allergic reaction
  - Purpose is to increase ***contrast*** of some tissue type
- Most commonly used is Gd-DTPA (Magnevist™)
  - Gadolinium ion (highly magnetizable) chelated to a molecule that won’t pass an intact blood-brain barrier
  - Makes T1-weighted images brighter where it accumulates and makes T2- and T2*-weighted images darker
- Deoxy-hemoglobin is an *endogenous* T2* agent

Tumor: T2 and T1+contrast

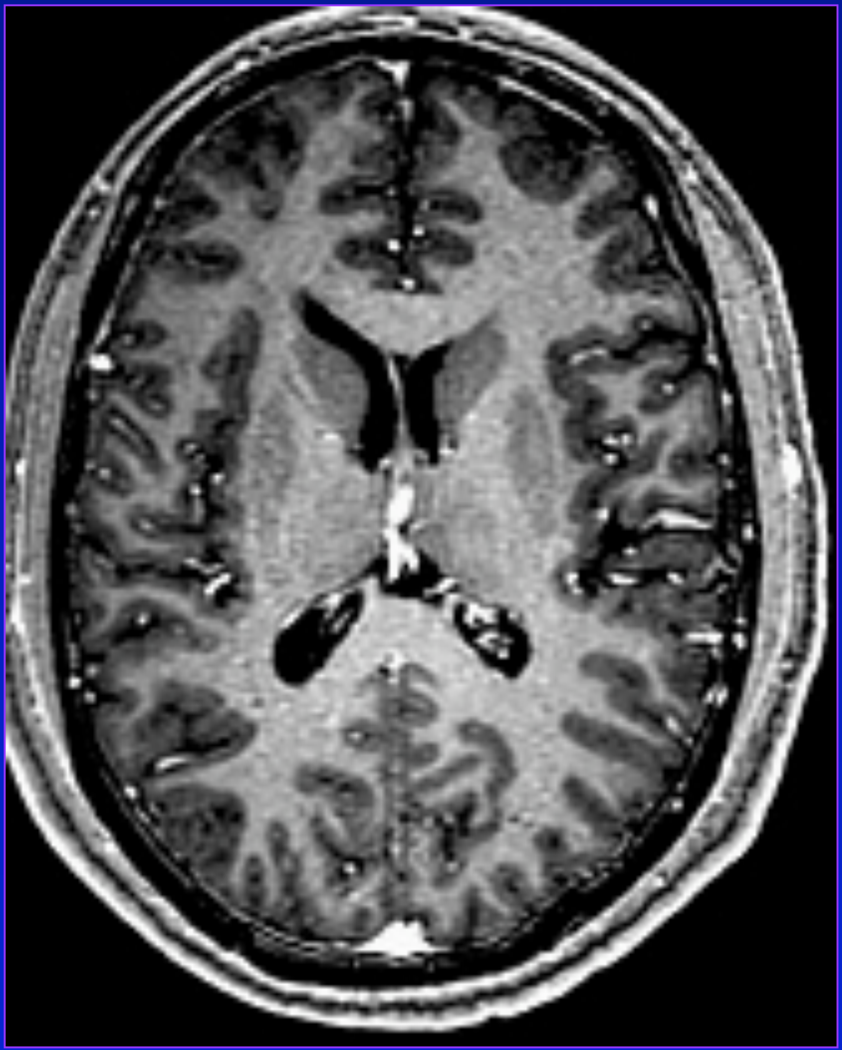


T2-weighted

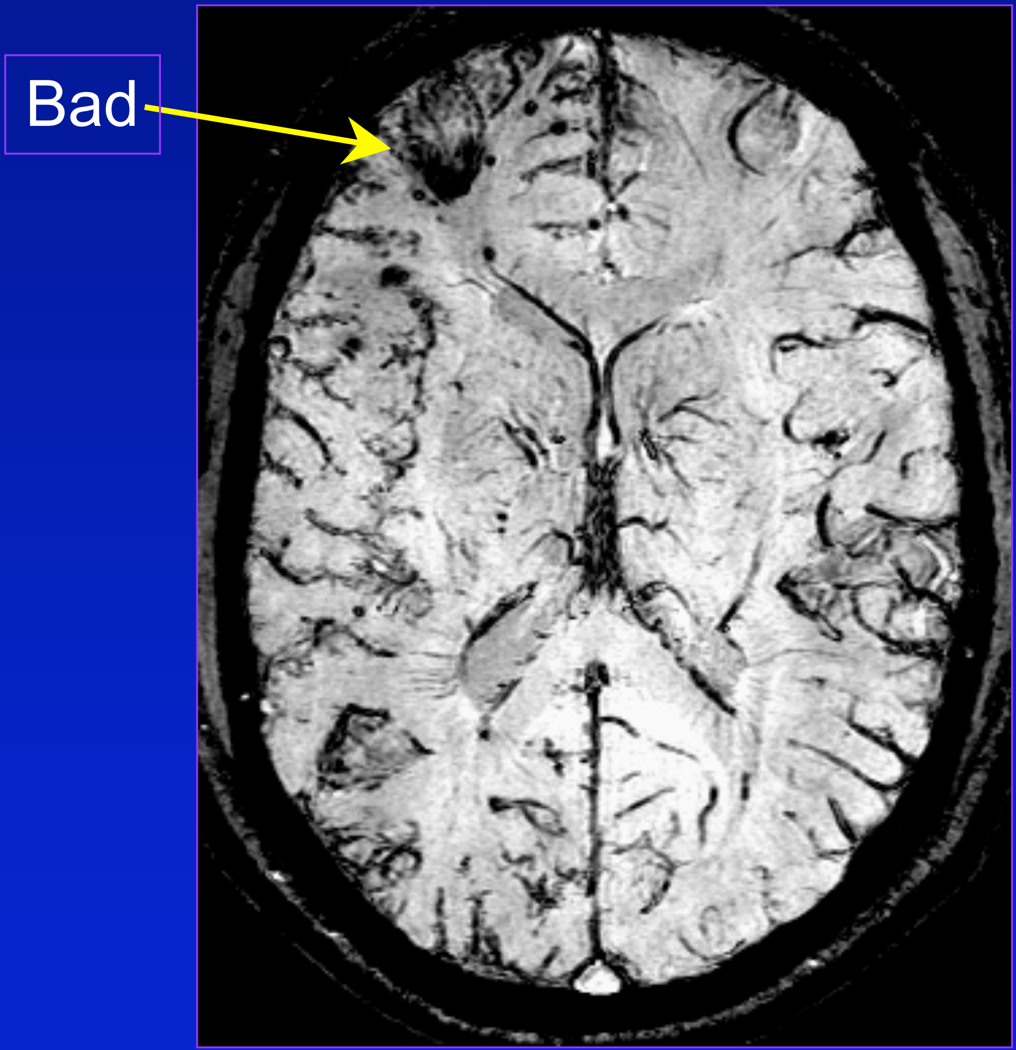


T1-weighted post-contrast

T2* MRV on a Seizure Patient



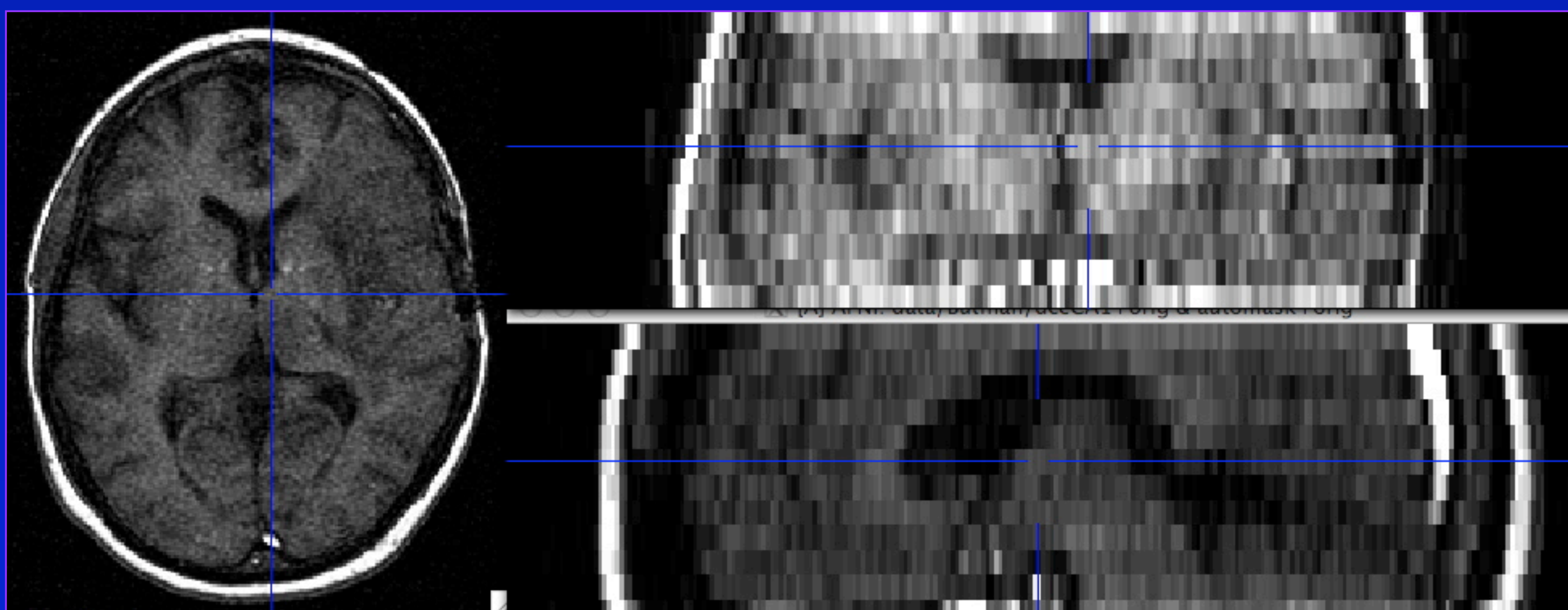
Gd-enhanced T1-weighted



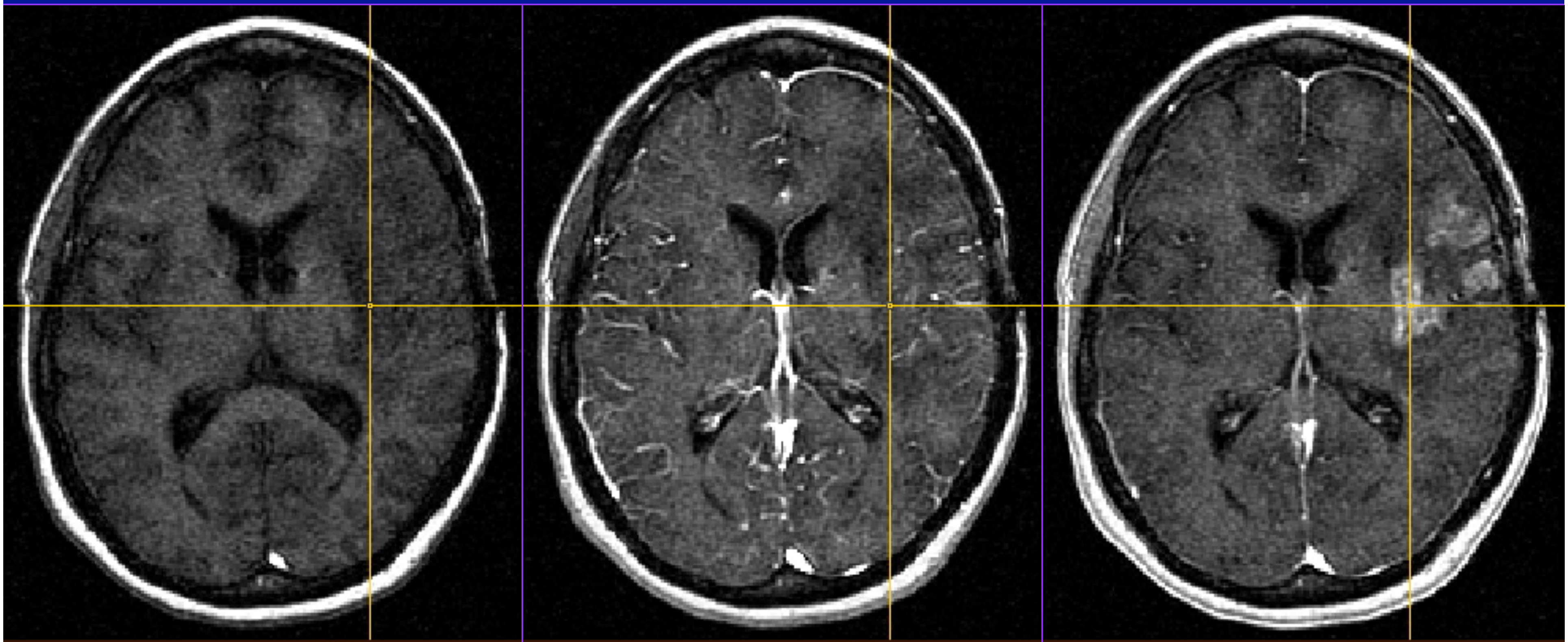
Gd-enhanced T2*-weighted

DCE-MRI and Brain Tumors

- DCE = Dynamic Contrast Enhancement
  - Inject contrast agent rapidly ("bolus") and take rapid images of brain repeatedly to observe its influx
  - Cost of taking such rapid images: coarser spatial resolution *and* limited spatial coverage *and* more noise
  - Below: rapid T1-weighted images (20 s per volume)
    - 12 slices at 5 mm thickness (0.9 mm in-slice resolution)



Time Series of Images



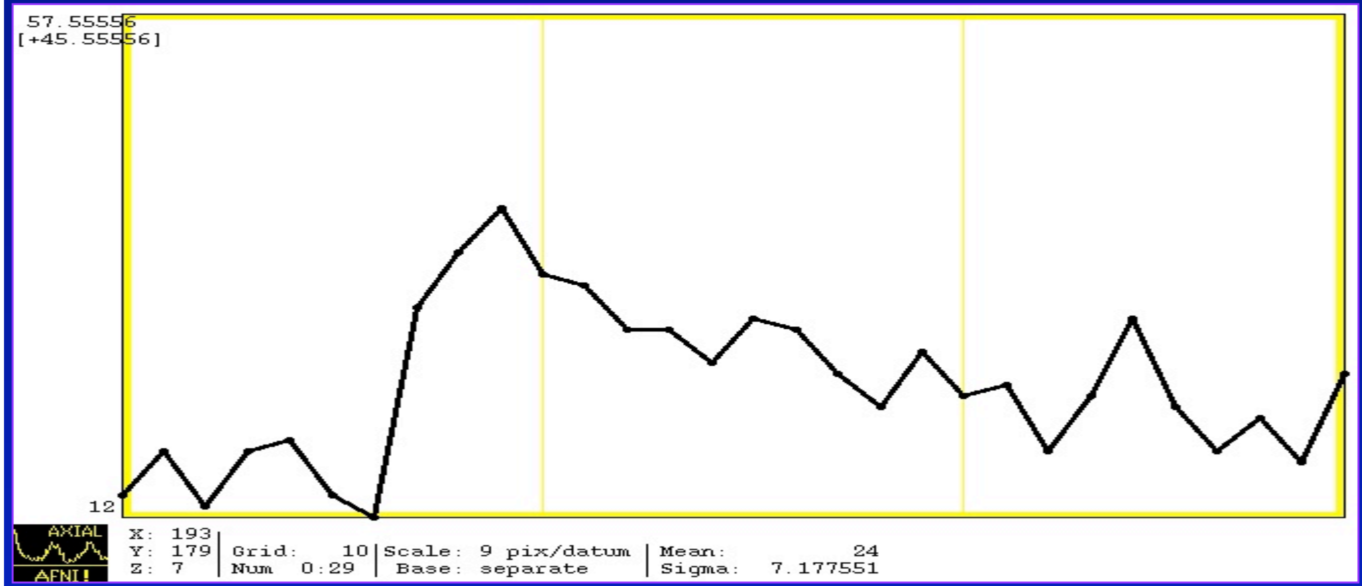
Time Point #7:
Before Gd hits
(bright spot =
sagittal sinus)

Time Point #9:
Gd into vessels

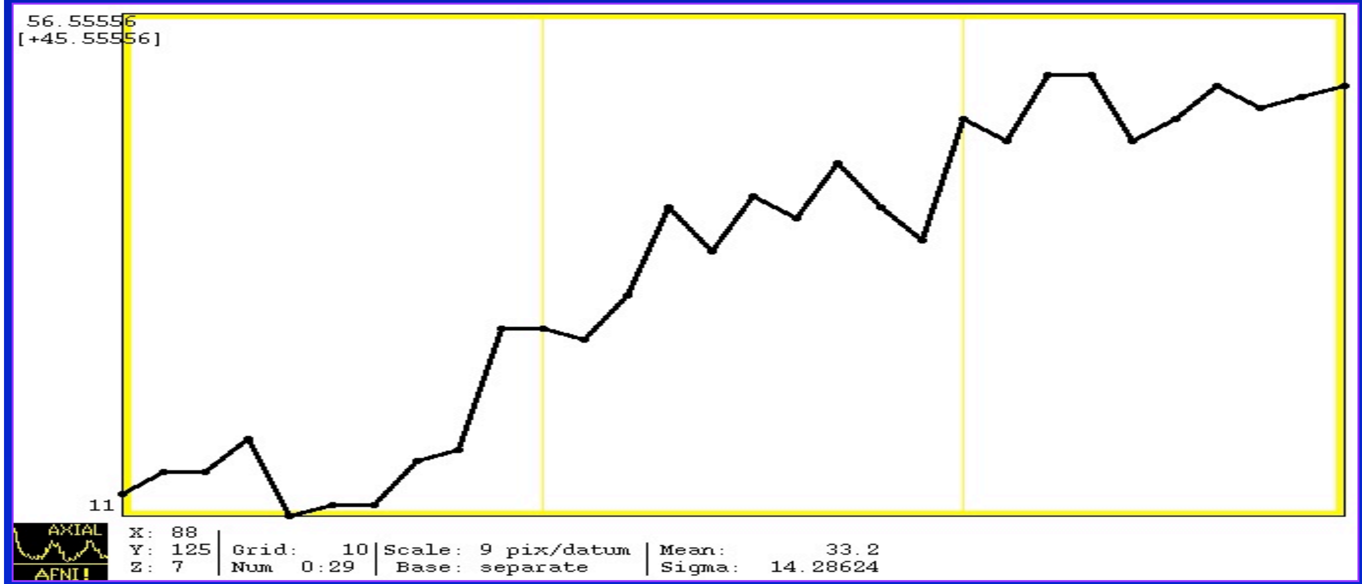
From John Butman's group in NIH/CC

Time Point #23:
Gd leaks into tumor
(now mostly gone
from vessels)

Time Courses of Voxel Intensities



- Voxel in vessel
  - This data is used as "arterial input function" for math model below



- Voxel in tumor
  - Can fit math model of Gd infiltration to quantify "leakiness"
  - Tumor grade?
  - Necrosis?
  - Treatment effects?

Diffusion Weighted Imaging

- Water molecules diffuse around during the imaging readout window of 10-100 ms
  - Scale of motion is 1-10 microns ≈ size of cells
  - Imaging can be made sensitive to this random diffusive motion (images are darkened where motion is larger)
- Can quantify diffusivity by taking an image without diffusion weighting and taking a separate image with diffusion weighting, then dividing the two:

$$\text{Image(no DWI)} \div \text{Image(with DW)} = e^{b \cdot D}$$

where *b* is a known factor and *D* is a coefficient that measures (apparent) diffusivity

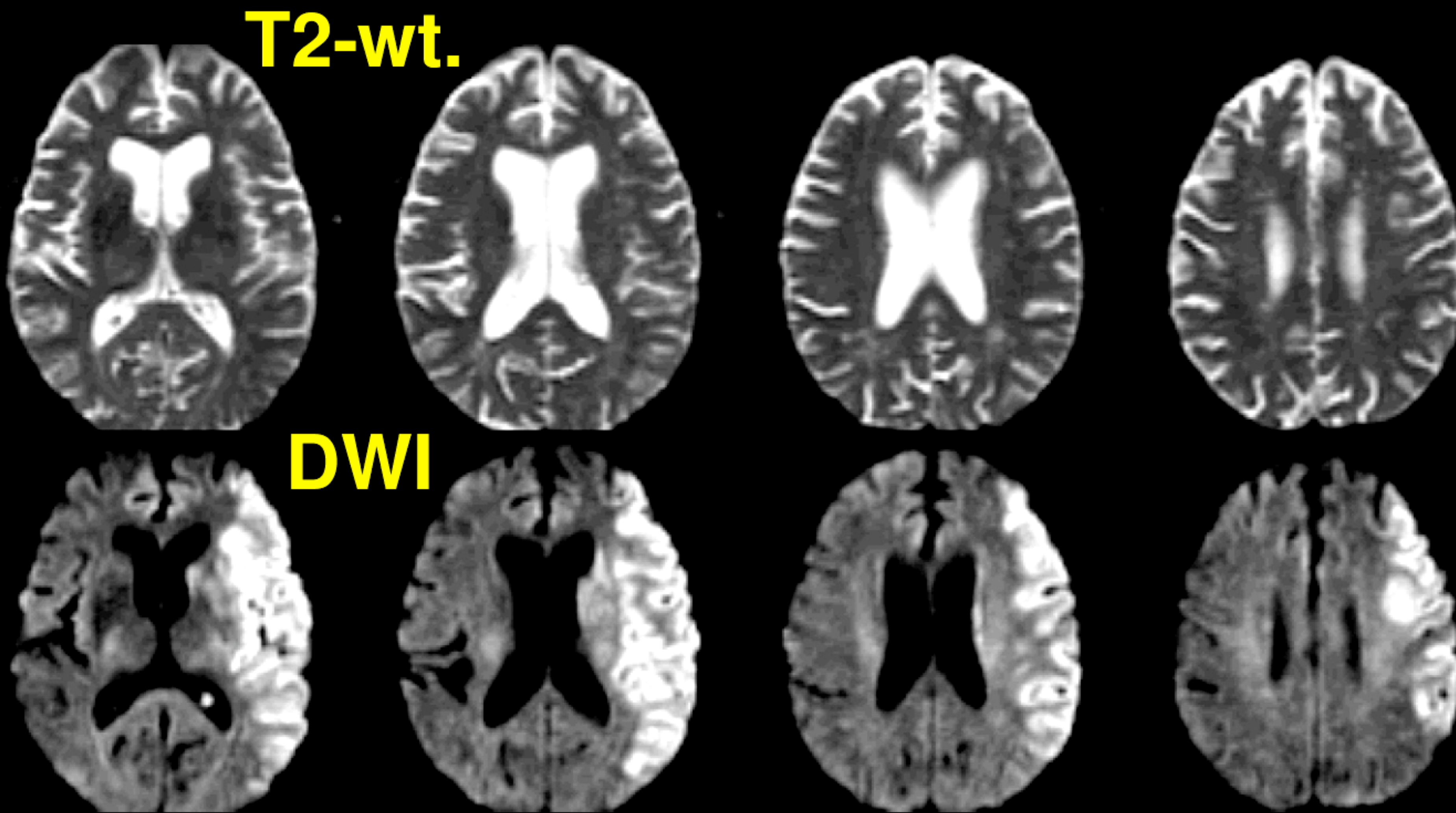
  - Can thus compute images of ADC from multiple (2+) scans

DWI in Stroke

- ADC decreases in infarcted brain tissue within *minutes* of the vessel blockage
    - Causes thought to include cell swelling shutting down water pores that allow easy $H_2 0$ exchange between intra- and extra-cellular spaces
    - Cell swelling also causes reduction in extra-cellular space which has a higher ADC than intra-cellular space
- Stroke damage doesn't show up on T1- or T2-weighted images for 2-3 *days* post-blockage
- DWI is now commonly used to assess region of damage in stroke emergencies
    - And whether to administer TPA (clot dissolving agent with many bad side-effects)

MRI and Acute Stroke

4 hours

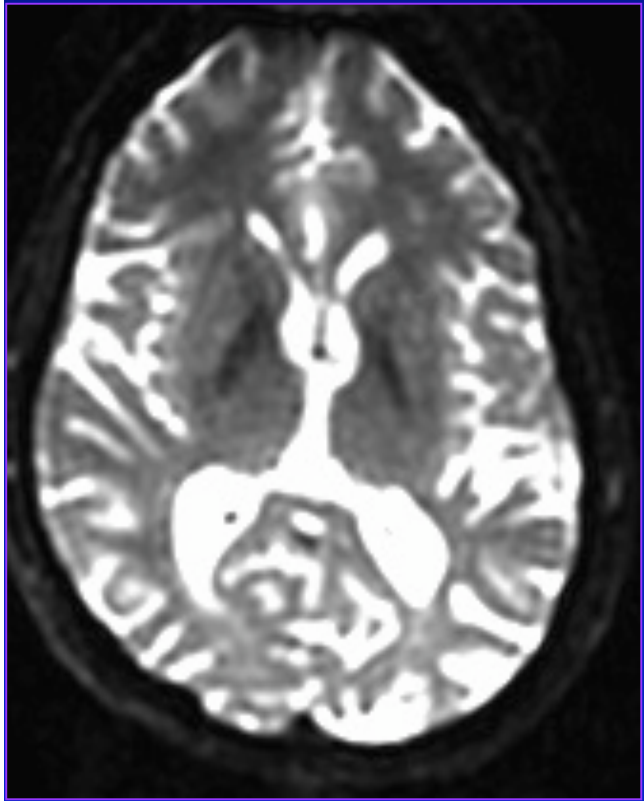


From Mike Mosely (Stanford Radiology)

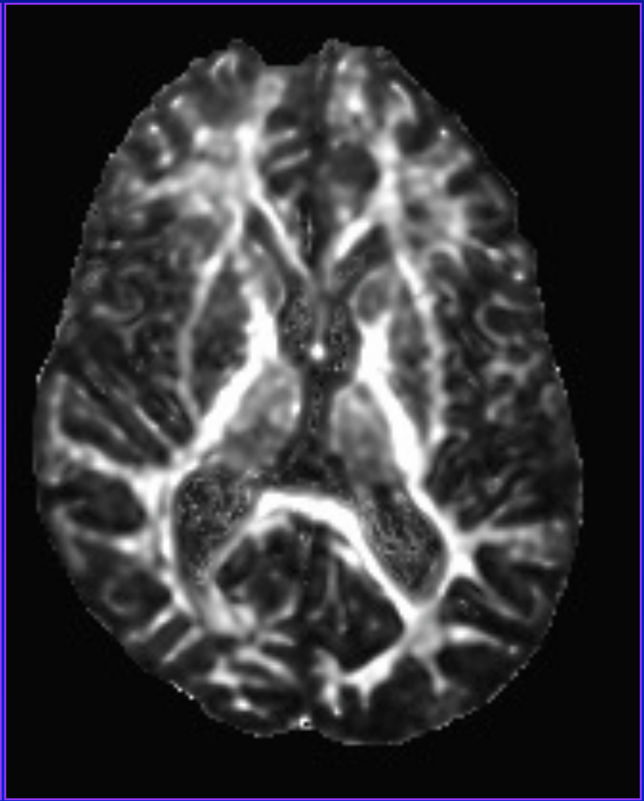
Diffusion Tensor Imaging

- Diffusive movement of water in brain is not necessarily the same in all directions — not isotropic
- In WM, diffusion transverse to axonal fiber orientation is much slower (3-5 times) than diffusion along fibers
  - This anisotropic diffusion is described mathematically by a *tensor* ≡ 3×3 symmetric matrix ≡ 3 perpendicular directions with 3 separate diffusion coefficients *D* along each one
- Diffusion weighted MR images can be designed to give more weight to diffusion in some directions than in others
- By acquiring a collection (7+) of images with different directional encodings, can compute the diffusion tensor in each voxel ⇒ WM fiber orientation

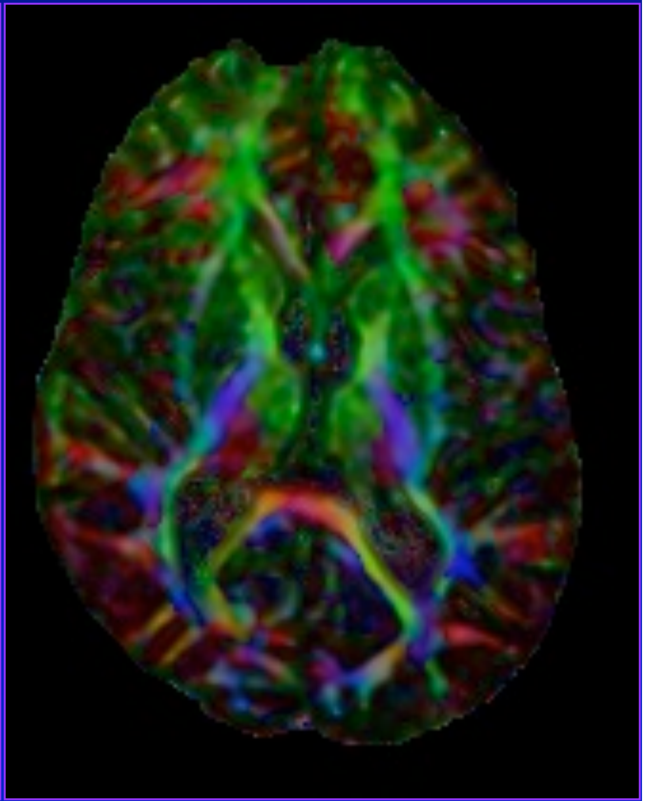
DTI Results



Unweighted (baseline b=0) image



Fractional Anisotropy (FA): Measures how much ADC depends on direction



FA Color-coded for fiber directionality:
x = Red y = Green
z = Blue

Other Types of MR Images

- MR Angiography = designed to enhance arterial blood (moving H_20) — sometimes with Gd contrast
  - Much more commonly used than MRV
  - Useful in diagnosing blood supply problems
- Magnetization Transfer = designed to indirectly image H in proteins (not normally visible in MRI) via their magnetic effects on magnetized H in water
  - Useful in diagnosing MS and ALS abnormalities in WM
    - Especially when used with Gd contrast agent
  - Possibly useful in detecting Alzheimer's plaques
- Perfusion weighted images = designed to image blood flow into capillaries only
- MRI methodology R&D continues to advance ….

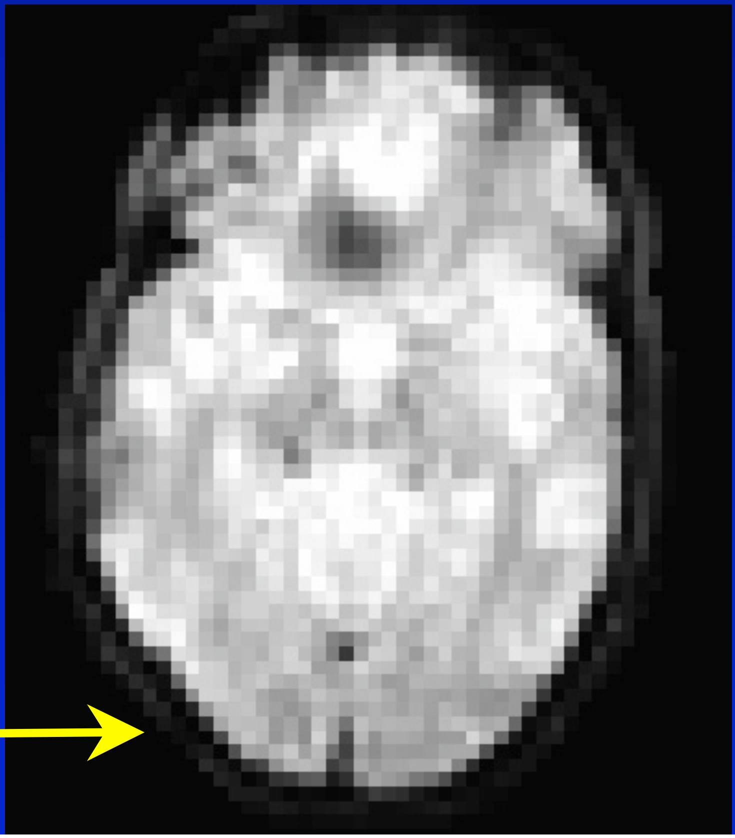
Functional Brain MRI - 1

- 1991: Discovery that oxygenation fraction of hemoglobin in blood changes *locally* (on the scale of 1-2 mm) about 2 seconds after increased neural activity in the region
- Recall T2*-weighted imaging: sensitive to deoxy-hemoglobin level in veins
  - Arterial blood is normally nearly 100% oxygenated
  - Resting state venous blood is about 50% oxygenated
  - Neural activation *increases* oxygenation state of venous blood (for various complicated reasons)
  - Since deoxy-hemoglobin makes T2*-weighted image darker, neural activation will make image brighter (because have less deoxy-hemoglobin) *locally*

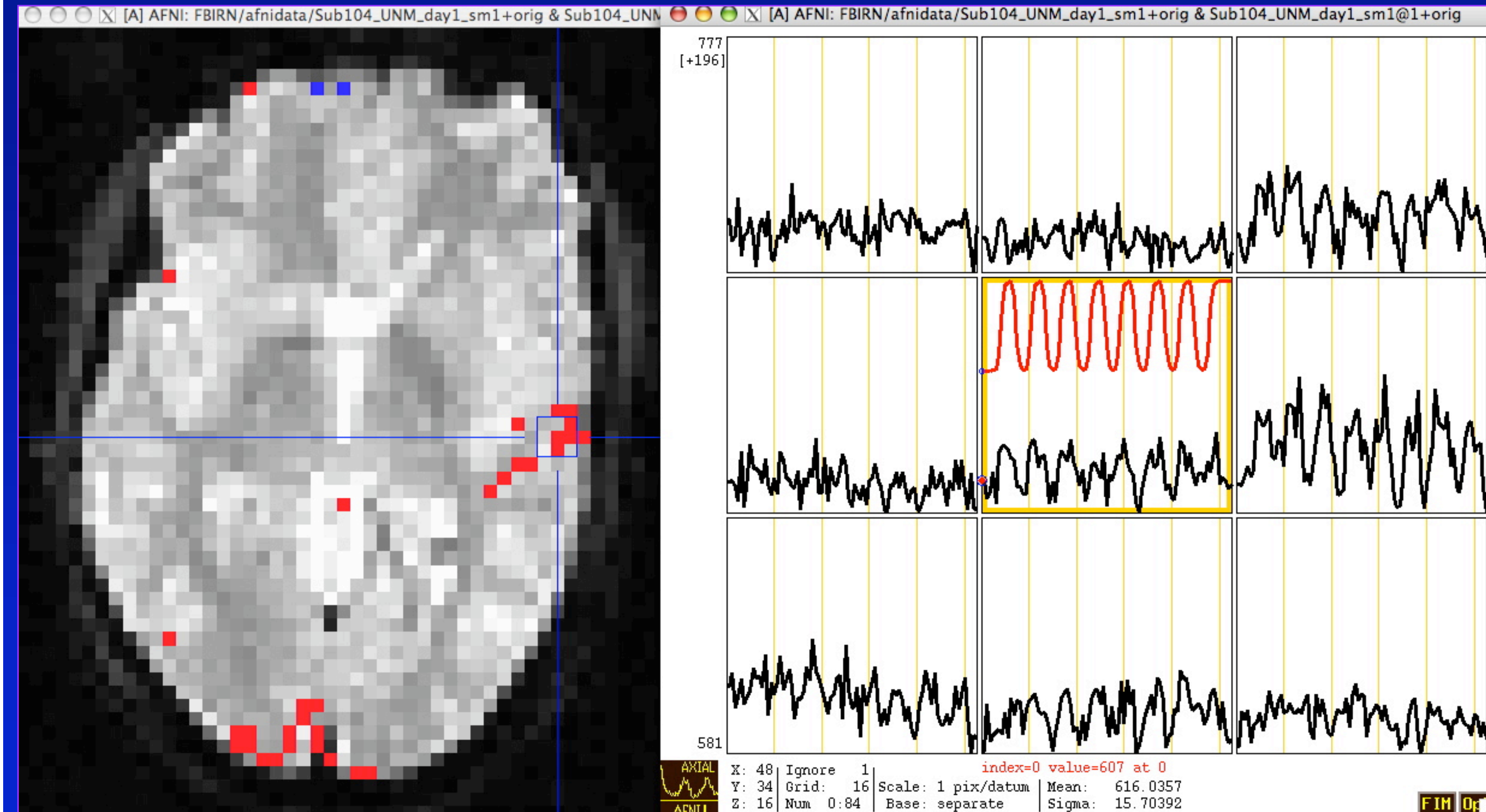
Functional Brain MRI - 2

- FMRI methodology:
  - Scan brain with T2*-weighted sequence every 2-3 seconds
  - Subject performs task in an on/off fashion, as cued by some sort of stimulus (visual, auditory, tactile, …)
  - Usually gather about 1000 brain volumes at low spatial resolution
  - Images look bad *in space*, but are designed to provide useful information through *time*
  - Analyze data time series to look for up-and-down signals that match the stimulus time series

A single fast (100 ms) 2D image

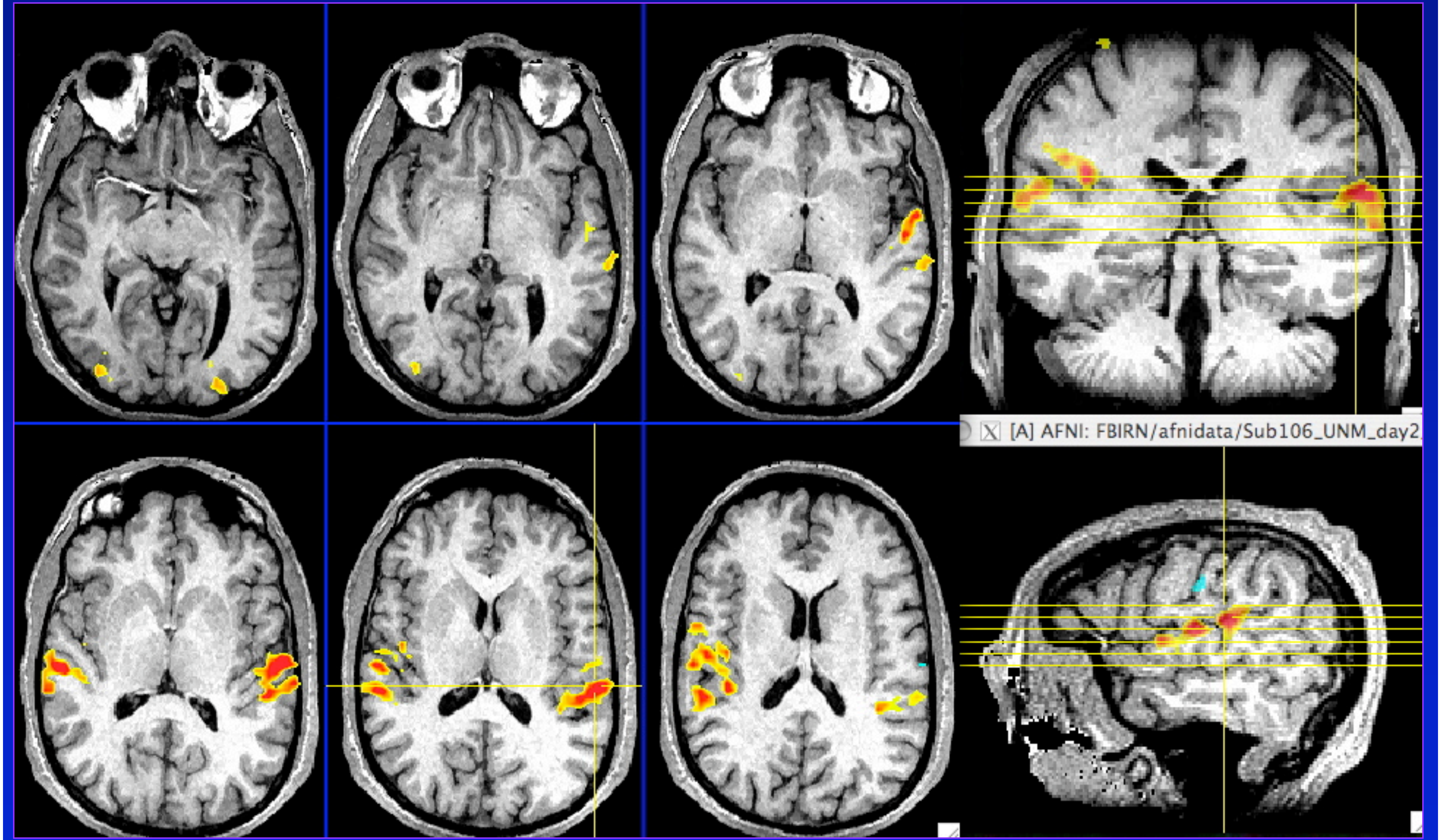


Functional Brain MRI - 3



One fast image *and* a 3×3 grid of voxel time series

Brain Activation Map



Time series analysis results overlaid on T1-weighted volume

Applications of FMRI

- Clinical (in individuals):
  - Pre-surgical mapping of eloquent cortex to help the surgeon avoid resecting viable tissue
  - Can combine with DTI to help surgeon avoid important white matter bundles (e.g., cortico-spinal tract)
  - Measure hemispheric lateralization of language prior to temporal lobe surgery for drug-resistant epilepsy
- Neuroscience (in groups of subjects):
  - Segregation of brain into separate functional units
    - What *are* the separate functions of the brain pieces-parts?
  - Discover differences in activity between patients and normals (e.g., in schizophrenia)
  - Map functional (i.e., temporal) connectivity
    - vs. anatomical connectivity (e.g., via DTI)

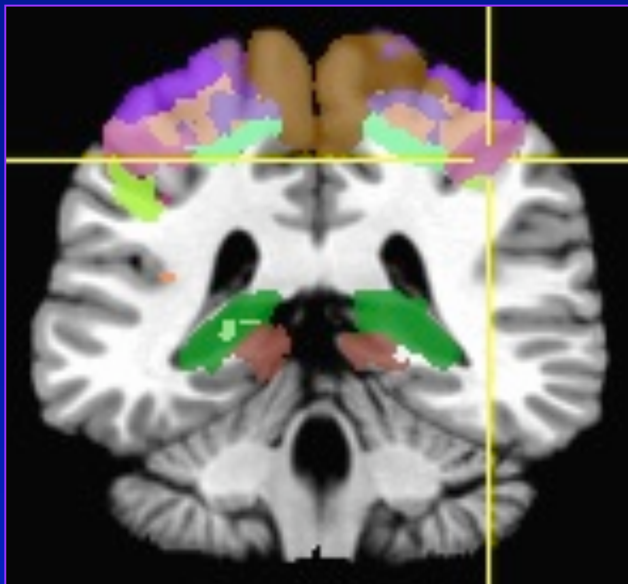
Other Brain Mapping Tools

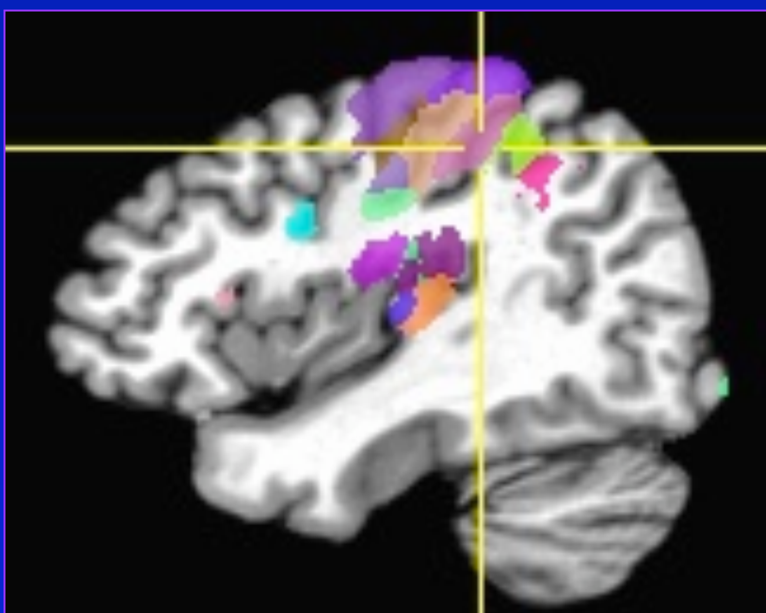
- Downsides to FMRI:
  - Poor time resolution since we are looking at signal from blood, not directly from neurons
  - Physiological connection between neural activity and hemodynamic signal measured by MRI is complex and poorly understood
- EEG and MEG: signal is from neural electrical activity, so time resolution is great
  - But spatial resolution is bad (and confusing)
- FDG PET: signal is closer to neural metabolism
  - But must give subject radioactive substance — limits repeat studies, etc.
  - Time resolution much worse than FMRI, and space resolution somewhat worse
- Through-the-skull IR: new-ish; hits brain surface region

Digital Brain Atlases

- Attempts to provide *statistical* localization on MRI scans of brain regions determined by post-mortem histology
  - Statistical because each person's brain is different in details
  - Major effort by Zilles' group in Jülich to categorize 10 brains, region by region, using histology
- Also available: Talairach & Tournoux atlas regional boundaries (derived from 1 brain in the 1980s, plus some literature search to clear up ambiguities in the published book) — from Fox's group at UT San Antonio
- These are the two freely available human brain atlas databases now distributed
  - Also are some privately held databases (corporate & academic)

Cyto-architectonic Atlas





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Focus point (LPI)=
     40 mm [R], -35 mm [P],  42 mm [S] {T-T Atlas}
     40 mm [R], -38 mm [P],  44 mm [S] {MNI Brain}
     42 mm [R], -38 mm [P],  51 mm [S] {MNI Anat.}

Atlas TT_Daemon: Talairach-Tournoux Atlas
   Focus point: Right Inferior Parietal Lobule
          -AND- Right Brodmann area 40
   Within 5 mm: Right Supramarginal Gyrus
   Within 6 mm: Right Postcentral Gyrus
   Within 7 mm: Right Brodmann area 2

Atlas CA_N27_MPM: Cytoarch. Max. Prob. Maps (N27)
   Focus point: Area 2
   Within 2 mm: hIP2
   Within 5 mm: Area 3b
   Within 7 mm: Area 3a
          -AND- Area 4p

Atlas CA_N27_ML: Macro Labels (N27)
   Focus point: Right Inferior Parietal Lobule
   Within 1 mm: Right Postcentral Gyrus
          -AND- Right SupraMarginal Gyrus

Atlas CA_N27_PM: Cytoarch. Probabilistic Maps (N27)
   Focus point: hIP2   (p = 0.20)
          -AND- Area 2   (p = 0.80)

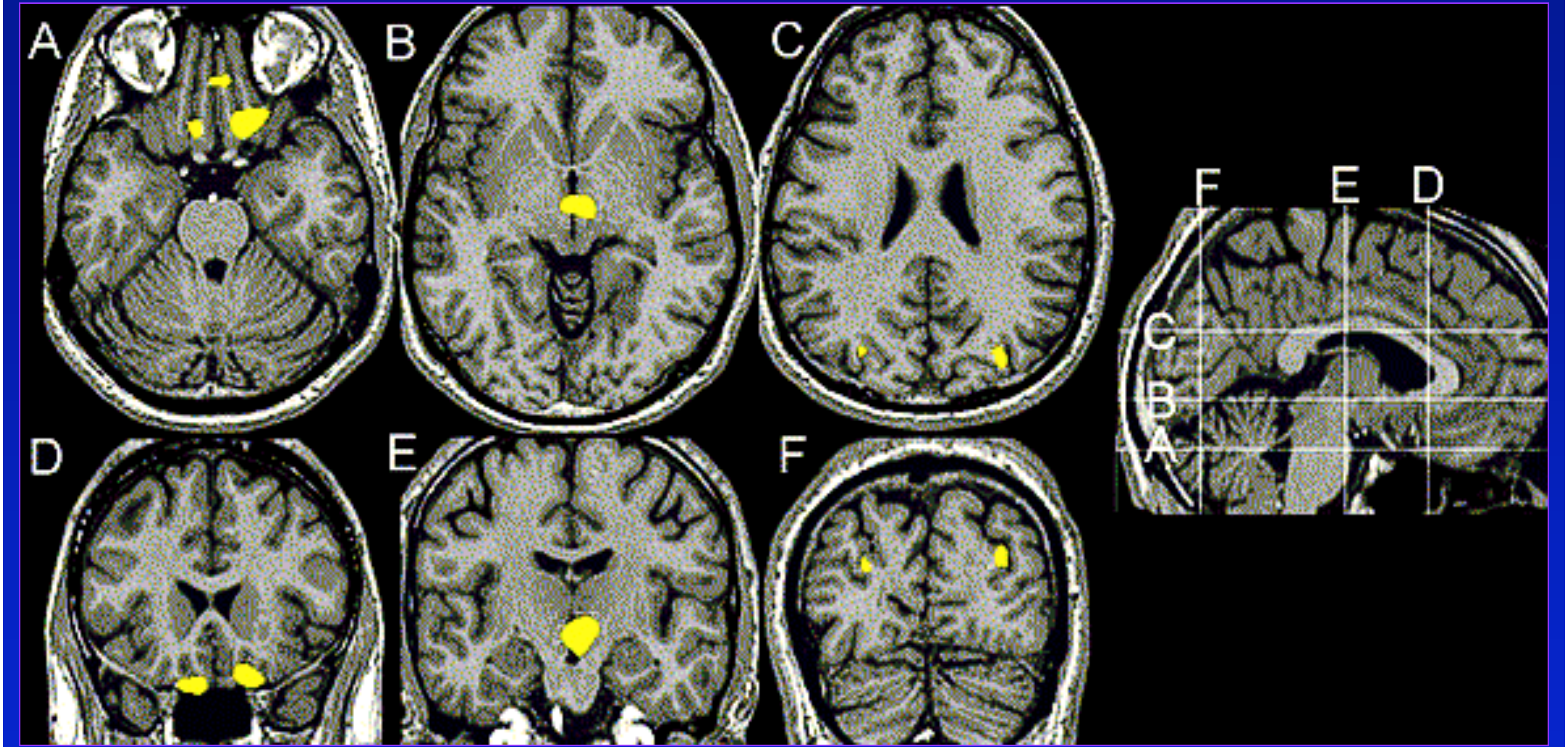
Atlas CA_N27_LR: Left/Right (N27)
   Focus point: Right Brain
```

"Where Am I" Navigation

Statistical Neuroanatomy

- Attempts to summarize and describe populations (and differences between populations) from MRI scans
- Example: Voxel Based Morphometry (VBM)
  - Try to characterize "gray matter density" as a function of location in brain, then map differences between patients and normals, …
  - Can also be applied to other measures (e.g., FA)
- Example: Cortical thickness maps
  - Extract gray matter cortical ribbon from images and measure thickness at each location
  - Map vs age, disease condition, …
- Biggest practical issue: ***Spatial Alignment***

VBM in Williams Syndrome



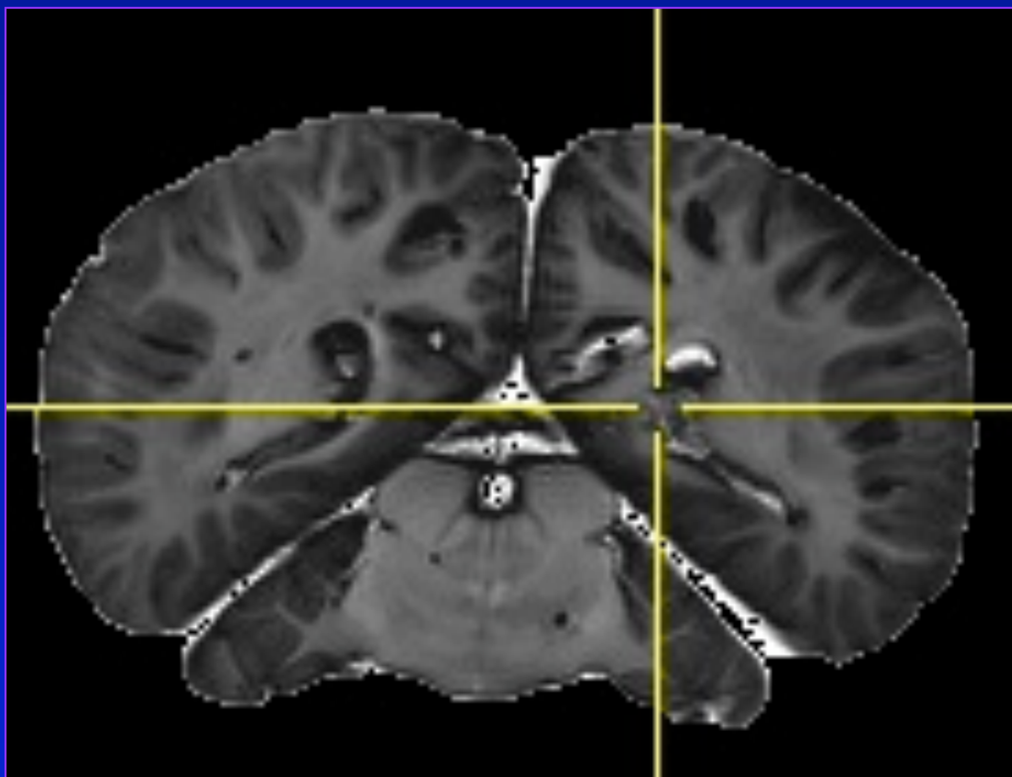
Yellow overlay shows regions with gray matter volume reduction in WS
(13 WS patients vs 11 normals)
From Karen Berman's group in NIMH

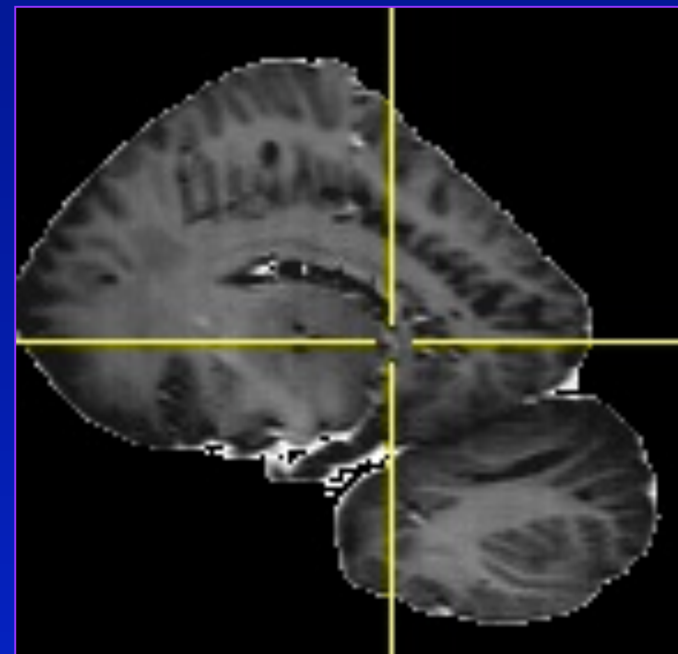
The End (almost)

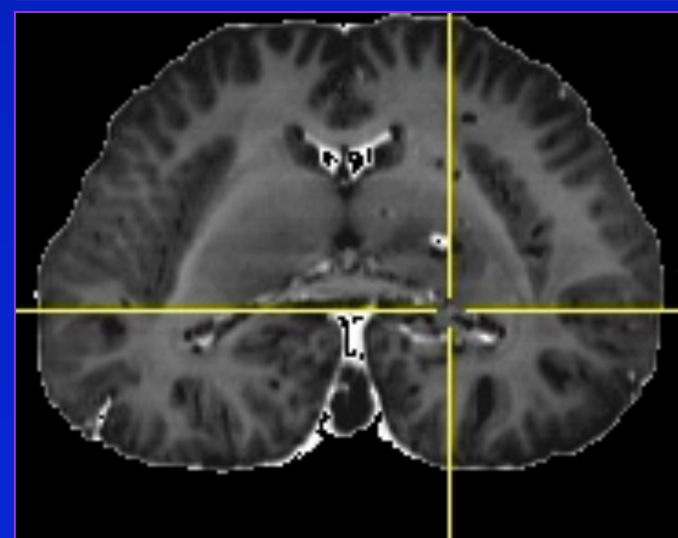
- MRI is:
  - Widely available (9000+ scanners in USA)
  - Harmless to subject ***if*** proper safety precautions are used
  - Very flexible: can make image intensity (contrast) sensitive to various sub-voxel structures
  - Still advancing in technology and applications
  - Still in a growth phase for brain research
- Limitations on spatial resolution and contrast types are frustrating
  - e.g., little chemical information is available with even the most sophisticated scanning methods
    - Novel contrast agents making some inroads in this direction

Unfair Pop Quiz

- What are these images of?







dolphin brain